Virology of Poliomyelitis

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SUMMARY

The virus of human poliomyelitis has been demonstrated in excretions before onset of the disease, during the disease, and in convalescence. It may be confused with different viruses likely to be found in the same sources in clinical conditions resembling poliomyelitis.

Immunologic differences between strains of poliomyelitis virus have been detected so that three types are now evident. The distribution of these types and their importance as causes of epidemics are not known. This multiplicity of immunologic types is an important factor in considering immunization of humans. Commercial manufacture of vaccines faces many technical problems.

Recently the Coxsackie virus has been demonstrated in humans with a disease closely resembling poliomyelitis.

THE infective agent of poliomyelitis has been defined in terms of its source, its pathogenicity for a limited host range, the pathologic and histologic features of the changes it causes in human and primate hosts, and its immunologic characteristics.[26] It has recently been given generic and specific names, *Legio debilitans*, in an effort to bring some order out of the chaos in the field of virus taxonomy.[5] This effort was probably not entirely justified by the stage of development of information on the subject. It is to be hoped, however, that this step will lead to the development of a more widely acceptable scheme of classification of the neurotropic viruses. This presentation will be largely confined to discussion of the virus of human poliomyelitis. Other viruses possibly of significance in human disease will be touched on briefly; the so-called Coxsackie virus will be discussed more especially.

Excretion of poliomyelitis virus during the course of infection and by carriers has been the subject of much important investigation in the past. The virus is demonstrable in the naso-oropharynx during four or five days prior to onset of symptoms and perhaps for as long as ten days after. It is also excreted in the feces for as long as four months after onset although less than 25 per cent of convalescent patients shed the virus past the sixth week.[28] The virus may be found in the feces some days prior to onset. The longest period so far observed was 19 days.[6] Where the virus is elaborated has not yet been determined. It has been demonstrated in the walls of the intestine and in mesenteric lymph nodes of experimental animals and of man.[34] It has also been found in tonsils.[17] The suggestion is strong that the wall of the alimentary tract is the primary site of invasion as well as the point of major excretion from the body. The virus has been demonstrated in peripheral nerves of experimental monkeys by electron micrography.[11] Children are more likely to excrete the virus than are adults, and the stools of young family contacts of patients are more liable to contain the virus than are the stools of adults of the family.[28] The virus was found in stools and throats of six out of ten patients with mild "summer grippe" occurring in an epidemic among children.[31] Recently, another virus, Coxsackie virus, has been isolated by inoculation of infant mice with pharyngeal and fecal excretions from patients who had symptoms closely resembling those of poliomyelitis.[9, 10] This agent has been detected in several sections of the country and like the poliomyelitis virus apparently has a wide geographic distribution.[8]

A number of other viruses have been described which resemble human poliomyelitis virus and which have been found under circumstances that allow of considerable doubt as to their etiologic connections with the human disease. Some confusion has been created in the past by the fact that some of these viruses have been regarded by certain workers as "models" of human poliomyelitis virus. The virus of mouse encephalomyelitis (Theiler virus), Columbia SK, MM, and encephalomyocarditis viruses can be listed in this group of infective agents.[26] They are probably primarily parasitic in lower animals, some occasionally attacking man, others probably never causing human disease.

Large scale investigation of the subject of differences that might exist among various strains of human poliomyelitis virus has for many years been hindered by the expense of experimental animals and the rather academic nature of the problem. Recently, however, greatly increased interest has been shown in the possibility of artificial immunization against the clinical disease, and as a consequence animals in plenty have become available for solution of a problem that may have retained its academic character but has acquired a very practical stature. Work on this problem during the past two or three years has brought to light that there

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are at least three major types or varieties of poliomyelitis which infect man.[1, 2, 3, 14, 16, 18, 23, 24, 30] Techniques include challenge of convalescent immune monkeys with large doses of viruses from different sources. By using two immunologically different viruses as prototypes, three types can be distinguished. Preliminary experiments with neutralization tests using serum from monkeys immunized with the prototypes have indicated that the same viruses fall in the same three types. Another technique in process of development has yet to be put to this use; this involves flocculation of purified viral antigens in specific immune sera, and the test is performed *in vitro*.[30] Yet to be determined (and of epidemiologic importance) is the geographic distribution of types over the world, the percentage occurrence of types in epidemics, and which types are to be found in carriers.

If vaccines capable of conferring adequate immunity are to be manufactured, distributed, and administered on a scale wide enough to curb the disease, several questions other than those regarding immunologic type differences must be answered. One is: Are killed or inactivated viruses immunogenic? Some work along this line[20, 22] indicates that formalinized virus preparations do provoke resistance to homologous test virus given intracerebrally. Another question is: How much overlapping immunity is produced by virus of one type as vaccine against another type? So far, indications are that little if any such cross-immunity is established, even with living vaccines,[1, 2, 3, 16, 18] although there is some suggestion that the death rate in animals paralyzed for a second time is lower than the rate in control groups (unpublished data). There is some evidence[25] that the immunity of infected animals is different from immunity of vaccinated animals and it has been suggested that this immunity to infection resides in the tissue of the central nervous system. This work has not yet been confirmed, however, so that the role of tissue antibody in resistance and even its existence are still in doubt.[32] Although considerable work has been done on the problem of attenuating or altering the virulence of a poliomyelitis virus to make it a safe vaccine in the manner of smallpox vaccine, yellow fever .vaccine, and others, no such product is immediately forthcoming. Another problem in the manufacture of a vaccine is its source. Spinal cords of infected monkeys have thus far served for experimental vaccines, but obviously this supply is too limited. Promise for solution of this problem is offered by the development of a technique for culture of human poliomyelitis virus in infantile human tissues, not restricted to nervous tissue and including skin.[12] This may lead to *in vitro* methods suitable for large-scale commercial production. The use of some chemical or physical method for purification and concentration of the virus would be a great help to settle the problem of source of vaccine. A recent report demonstrated that poliomyelitis virus can be concentrated to some extent and somewhat freed of extraneous brain tissue material by processing with protamine sulfate.[35] The problem of demyelinating encephalomyelitis as a postvaccinal complication will necessitate use of methods to remove the encephalitogenic factor from vaccine made from central nervous system tissue. This problem is under active investigation in connection with rabies vaccine manufacture, and a recent report states that some success has been achieved in an experimental method for removing the troublesome fraction.[13]

Problems presented by this disease have been enhanced recently by the discovery of another viral agent (previously mentioned) which is present in secretions of the nose and throat and in feces[9, 10] of patients with paralytic or non-paralytic disease resembling poliomyelitis. This agent was found in feces of non-paralytic patients during an epidemic of poliomyelitis.[8] It was also found in the feces of some of the previously mentioned patients with "summer grippe"; and when monkeys were inoculated with preparations from the feces of those patients, typical poliomyelitis virus was recovered from the monkeys. So the two viruses may co-exist.[21a] Accidental laboratory infections with this virus have resulted in a disease with symptoms of pleurodynia. Neutralizing antibodies developing during convalescence are distinguishable from antipoliomyelitis antibodies. Five antigenic types of the virus have been defined on the basis of complement-fixation tests.[7, 15, 33] The influence of these findings on the future control of poliomyelitis cannot yet be assessed. Monkeys are not infected experimentally with this virus except for the cynomolgous monkey, in which a mild disease resembling experimental non-paralytic poliomyelitis develops.[21]

Thus, a more thorough understanding of the virology of poliomyelitis is necessary for an intelligent approach to the problems of the control of the disease. And at present data are being gathered in various cooperating and also independently operating laboratories in order that this goal may be achieved.

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